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SEARCH REQUEST FORM

4 11

Requestor's Name: S. Devi

Serial Number: 08/870,762

Date: 1 April 98 Phone: 308-1347 Art Unit: 1641

Search Topic:
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please perform a search on the attached claims.
Please include foreign patent data bases.
Inventor names and key words and synonyms are provided in the attached sheet.

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PTO-1590 (9-90)

WE CLAIM:

1. A method of treating or preventing obesity in a human subject comprising administering to said subject an effective amount of an amylin or an amylin agonist.

2. A method according to claim 1 wherein said amylin agonist is an amylin agonist analogue.

3. A method according to claim 2 wherein said amylin agonist analogue is ^{25,28,29}Pro-h-amylin.

4. A method according to claim 1 wherein said amylin or amylin agonist is administered subcutaneously.

5. A method according to claim 4 wherein said amylin or amylin agonist is administered from 1 to 4 times per day.

6. A method according to claim 5 wherein said amylin or amylin agonist is administered in an amount from 30 μg/dose to 300 μg/dose.

Searched - Serialized - Indexed

Case: 08/870,762

Key words for the search:

1) Amylin or DAP or diabetes associated protein
2) Amylin agonist or amylin agonist analogue or pramlintide or AC-0137 or ^{24,28,29}Pro-h-amylin or ^{18} Arg ^{24,28,29}Pro-h-amylin or ^{18} Arg ^{25,28}Pro-h-amylin or AC187

The key word Amylin should be hooked with: a) Diabetes; 2) Obesity; 3) Vasodilation; 4) Hyperglycemic peptide during the search.

Inventor search: 1) Bradford Duft
2) Orville Kolterman

S. DEVI
870762

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=> fil reg

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=> e amylin/cn 5

E1            1      AMYLHYDROQUINONE/CN
E2            1      AMYLHYDROXYBENZENE/CN
E3            1 --> AMYLIN/CN
E4            1      AMYLIN (38-TYROSINE) (HUMAN OXIDIZED)/CN
E5            1      AMYLIN (CANINE REDUCED)/CN

=> s amylin ?/cn

L1           32 AMYLIN ?/CN

=> s "25,28,29pro-h-amylin"

             0 "25,28,29PRO"
        134799 "H"
            90 "AMYLIN"
L2           0 "25,28,29PRO-H-AMYLIN"
                 ("25,28,29PRO"(W)"H"(W)"AMYLIN")

=> s "25,28,29 pro-h-amylin"

             0 "25,28,29"
          5218 "PRO"
            54 "PROS"
          5272 "PRO"
                 ("PRO" OR "PROS")
        134799 "H"
            90 "AMYLIN"
L3           0 "25,28,29 PRO-H-AMYLIN"
                 ("25,28,29"(W)"PRO"(W)"H"(W)"AMYLIN")

=> s "pro-h-amylin"/cn

L4           0 "PRO-H-AMYLIN"/CN

=> e dap/cn 5

E1           1      DAOTAN VTW 2229/CN
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E2            1      DAOTHAN 1226/CN
E3            4 --> DAP/CN
E4            1      DAP (AMINE)/CN
E5            1      DAP (PESTICIDE)/CN

=> s e3

L5            4 DAP/CN

=> s diabetes associated protein/cn 5

MISSING OPERATOR

=> s diabetes associated protein/cn

L6            0 DIABETES ASSOCIATED PROTEIN/CN

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=> s (l1 or amylin or dap or diabetes associated protein or pro(3w)amylin or
ac(w)(0137 or 187)) and (diabet? or obesi? or vasodil? or hyperglycem?)

L7          310 FILE CAPLUS
L8          341 FILE BIOSIS
L9          390 FILE MEDLINE
L10         332 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
L11          42 FILE WPIDS
L12          92 FILE USPATFULL

TOTAL FOR ALL FILES
L13        1507 (L1 OR AMYLIN OR DAP OR DIABETES ASSOCIATED PROTEIN OR
                PRO(3W) AMYLIN OR AC(W)(0137 OR 187)) AND (DIABET? OR
                OBESI? OR VASODIL? OR HYPERGLYCEM?)

=> s l13 and (duft b? or kolterman o?)/au,in

L14           5 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L15          12 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L16           8 FILE MEDLINE
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'IN' IS NOT A VALID FIELD CODE
L17 8 FILE EMBASE
L18 2 FILE WPIDS
L19 0 FILE USPATFULL

TOTAL FOR ALL FILES
L20 35 L13 AND (DUFT B? OR KOLTERMAN O?)/AU,IN

=> dup rem l20

PROCESSING COMPLETED FOR L20
L21 21 DUP REM L20 (14 DUPLICATES REMOVED)

=> d 1-21 cbib abs;s (obes? or overweight) and (l1 or amylin?)

Adolphi RC660.A1 D53

L21 ANSWER 1 OF 21 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1
1997:718438 Document No. 127:341630 Effects of 4 weeks' administration of pramlintide, a human **amylin** analog, on glycemia control in patients with IDDM. Effects on plasma glucose profiles and serum fructosamine concentrations. Thompson, R. G.; Pearson, L.; **Kolterman, O. G.** (Amylin Pharmaceuticals Inc., San Diego, CA, 92121, USA). Diabetologia, 40(11), 1278-1285 (English) 1997. CODEN: DBTGAJ. ISSN: 0012-186X. Publisher: Springer.

Type 1.

AB The effects of 4 wk' administration of pramlintide, an analog of the human hormone **amylin**, on blood glucose control in patients with insulin-dependent **diabetes** mellitus were examd. Pramlintide was administered s.c. prior to meals in 4 dosing regimens: 30 .mu.g 4 times per day (breakfast, lunch, dinner, and evening snack[BLDE]), 30 .mu.g 3 times per day (breakfast, lunch and dinner [BLD]), 30 .mu.g 3 times per day (breakfast, dinner and evening snack [BDS]), and 60 .mu.g twice per day (breakfast and dinner[BD]). After 4 wk of pramlintide 30 .mu.g 4 times per day administration, there was a redn. in the mean 24 h blood plasma glucose concn. when compared to placebo (- 1.4 vs 0.3 .mu.mol/L). Serum fructosamine concns. were reduced 62 .mu.mol/L (BLDE), 43 .mu.mol/L (BLD), 47 .mu.mol/L (BDS), 46 .mu.mol/L (BD), and 29 .mu.mol/L (placebo). The incidence of hypoglycemia was not different in any pramlintide group compared to the placebo group. Nausea, the most frequent adverse event, subsided after the 1st week of treatment in the majority of patients. In conclusion, pramlintide improved blood glucose control over a 4-wk period without increased hypoglycemia and was well tolerated.

L21 ANSWER 2 OF 21 MEDLINE DUPLICATE 2
97366562 Document Number: 97366562. Pramlintide: a human **amylin** analogue reduced postprandial plasma glucose, insulin, and C-peptide concentrations in patients with type 2 **diabetes**. Thompson R G; Gottlieb A; Organ K; Koda J; Kisicki J; **Kolterman O G**. (Amylin Pharmaceuticals, Inc., San Diego, California 92121, USA.)DIABETIC MEDICINE, (1997 Jul) 14 (7) 547-55. Journal code: DME. ISSN: 0742-3071. Pub. country: ENGLAND: United Kingdom. Language: English.

X, P

AB In order to determine the influence of a 5 h infusion of pramlintide compared to placebo on postprandial glucose, lactate, insulin, and C-peptide concentrations in patients with Type 2 **diabetes**, a single-blind, randomized, cross-over study was conducted in 24 patients; 12 treated with exogenous insulin and 12 managed with diet and/or oral hypoglycaemic agents. One hour after initiation of infusion, patients consumed a Sustacal test meal. The protocol was repeated on the following day with each patient receiving the

alternate study medication. Pramlintide infusion in the insulin-treated patients resulted in statistically significant reductions in mean glucose, insulin, C-peptide, and lactate concentrations during the 4-h period after the Sustacal test meal. Pramlintide infusion also resulted in significant reductions of mean insulin, C-peptide, and lactate concentrations, but not glucose concentrations, in the patients treated with diet and/or oral hypoglycaemic agents. Within this latter group, reduction in postprandial glucose concentrations in individual patients correlated with glycated haemoglobin values. These results suggest that administration of pramlintide may improve glycaemic control in patients with Type 2 **diabetes** treated with insulin or poorly controlled on diet and/or oral hypoglycaemic agents.

L21 ANSWER 3 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
97:371676 Document No.: 99670879. Effects of the **amylin** analogue pramlintide on the glucose response to a glucagon challenge in IDDM.. Orskov L; Nyholm B; Hove K Y; Gravholt C H; Moller N; **Kolterman O**; Alberti K G M M; Schmitz O. Dep. Med. C, Univ. Hosp. Aarhus, Aarhus, Denmark Diabetologia16th International Diabetes Federation Congress, Helsinki, Finland, July 20-25, 1997., 40 (SUPPL. 1). 1997. A355. ISSN: 0012-186X. Language: English
AN 97:371676 BIOSIS

L21 ANSWER 4 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
97:371677 Document No.: 99670880. Pramlintide improves glycemic control in patients with type II **diabetes** requiring insulin.. Thompson R; Pearson L; Schoenfeld S; **Kolterman O** . Amylin Pharmaceuticals Inc., San Diego, CA, USA Diabetologia16th International Diabetes Federation Congress, Helsinki, Finland, July 20-25, 1997., 40 (SUPPL. 1). 1997. A355. ISSN: 0012-186X. Language: English
AN 97:371677 BIOSIS

L21 ANSWER 5 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
97:371678 Document No.: 99670881. The human **amylin** analogue pramlintide inhibited glucagon secretion in type I **diabetic** subjects.. Fineman M S; **Kolterman O G**; Thomspon R G; Koda J E. Diabetologia16th International Diabetes Federation Congress, Helsinki, Finland, July 20-25, 1997., 40 (SUPPL. 1). 1997. A355. ISSN: 0012-186X. Language: English
AN 97:371678 BIOSIS

L21 ANSWER 6 OF 21 MEDLINE
97355847 Document Number: 97355847. **Amylin** and glycaemic regulation: a possible role for the human **amylin** analogue pramlintide. **Kolterman O G**. (Amylin Pharmaceuticals Inc., San Diego, CA 92121, USA.)DIABETIC MEDICINE, (1997 Jun) 14 Suppl 2 S35-8. Ref: 20. Journal code: DME. ISSN: 0742-3071. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Clinical studies with the human **amylin** analogue, pramlintide, suggest that it may help to improve glycaemic control in patients with **diabetes** mellitus using insulin. This has been demonstrated by reductions in postprandial glycaemic excursion, 24-h glucose profile and serum fructosamine concentrations following administration of pramlintide for periods of up to 28 days in patients with Type 1 **diabetes**. Additionally, preliminary studies with pramlintide in patients with Type 2 **diabetes** using insulin have indicated its ability to reduce postprandial hyperglycaemia in this population. Thus, this data set suggests a potential role for pramlintide as a partner to insulin for the

Date June 13

optimization of glycaemic control in patients with **diabetes** using insulin.

L21 ANSWER 7 OF 21 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
97223996 EMBASE **Amylin** and glycaemic regulation: A possible role for the human **amylin** analogue pramlintide.
Kolterman O.G.. Dr. O.G. Kolterman, Amylin Pharmaceuticals Inc., 9373 Towne Centre Drive, San Diego, CA 92121, United States.
Diabetic Medicine 14/SUPPL. 2 (S35-S38) 1997.
Refs: 20.
ISSN: 0742-3071. CODEN: DIMEEV. Pub. Country: United Kingdom.
Language: English. Summary Language: English.
AB Clinical studies with the human **amylin** analogue, pramlintide, suggest that it may help to improve glycaemic control in patients with **diabetes** mellitus using insulin. This has been demonstrated by reductions in postprandial glycaemic excursion, 24-h glucose profile and serum fructosamine concentrations following administration of pramlintide for periods of up to 28 days in patients with Type 1 **diabetes**. Additionally, preliminary studies with pramlintide in patients with Type 2 **diabetes** using insulin have indicated its ability to reduce postprandial hyperglycaemia in this population. Thus, this data set suggests a potential role for pramlintide as a partner to insulin for the optimization of glycaemic control in patients with **diabetes** using insulin.

L21 ANSWER 8 OF 21 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 3
1997:111186 Document No. 126:113183 Treatment of type II **diabetes** mellitus with **amylin** agonists.
Kolterman, Orville G.; Thompson, Robert G.; Mullane, John F. (Amylin Pharmaceuticals, Inc., USA; Kolterman, Orville G.; Thompson, Robert G.; Mullane, John F.). PCT Int. Appl. WO 9640220 A1 961219, 35 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 96-US9875 960607. PRIORITY: US 95-483188 950607.
AB Methods for treating non-insulin-taking Type II **diabetes** mellitus are disclosed which comprise administering a therapeutically effective amt. of an **amylin** agonist. Results of a clin. trial testing the effects of AC137 (25,28,29Pro-h-**amylin**) are described.

L21 ANSWER 9 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 4
96:328410 Document No.: 99050766. Effect of race and hypertension on plasma **amylin** concentrations.. Dimsdale J E; **Kolterman O**; Koda J; Nelesen R. UCSD, La Jolla, CA 92093-0804, USA Hypertension (Dallas), 27 (6). 1996. 1273-1276.
ISSN: 0194-911X. Language: English
AN 96:328410 BIOSIS
AB **Amylin** is a recently discovered peptide hormone composed of 37 amino acids that is cosecreted with insulin by pancreatic beta cells. **Amylin** has been reported to be present in increased amounts in insulin-resistant subjects who are hyperinsulinemic. Because blacks and whites differ in the prevalence of both hypertension and **diabetes**, we examined **amylin** levels in 77 individuals; 42 were black (11 hypertensive and 31 normotensive) and 35 were white (10 hypertensive and 25 normotensive) individuals who were either healthy control subjects or hypertensive

subjects not receiving antihypertensive medication. Plasma **amylin** concentrations were measured in two separate monoclonal antibody-based immunofluorescent sandwich-type assays. The F002-2 capture antibody binds **amylin** plus at least two additional **amylin**-like peptides, and the F024-4 capture antibody detectably binds only the **amylin** peptide. There was a significant race-by-diagnosis interaction for levels of **amylin** immunoreactivity during a 2-hour glucose tolerance test (P lt .005 for F002-2 antibody and P lt .05 for F024-4 antibody). Highest levels were found in black hypertensive subjects. The results appear to fit with previously observed differences in metabolic status between blacks and whites and with the association between hypertension and alterations in metabolic status.

L21 ANSWER 10 OF 21 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 5
1996:258292 Document No. 124:332611 Effect of 14 days' subcutaneous administration of the human **amylin** analog, pramlintide (AC137), on an intravenous insulin challenge and response to a standard liquid meal in patients with IDDM. **Kolterman, O. G.**; Schwartz, S.; Corder, C.; Levy, B.; Klaff, L.; Peterson, J.; Gottlieb, A. (Amylin Pharmaceuticals, Inc.,, San Diego, CA, 92121, USA). Diabetologia, 39(4), 492-9 (English) 1996. CODEN: DBTGAJ. ISSN: 0012-186X.

AB Individuals with insulin-dependent **diabetes** mellitus (IDDM or type 1 **diabetes**) are deficient in both insulin and **amylin**, peptides secreted by the beta cell. We have investigated the effects of **amylin** replacement therapy employing the human **amylin** analog, pramlintide (25, 28, 29-**pro**-human **amylin**, previously referred to as AC137), upon the responses to a standardized insulin infusion (40 mU .sum. kg-1 .sum. h-1) for 100 min and a liq. Sustacal meal (360 kcal) in 84 healthy IDDM patients. Following baseline evaluations, patients were randomly assigned to receive s.c. injections of placebo, 30, 100 or 300 .mu.g pramlintide 30 min before meals for 14 days. There was no meaningful difference between adverse events reported by the 30-.mu.g pramlintide and the placebo groups, but ten subjects withdrew due to nausea, eight of these in the 300-.mu.g dose group. Peak plasma pramlintide concns. for the 30-.mu.g group were 21 .+-. 3 and 29 .+-. 5 pmol/l on Days 1 and 14, resp. These values are similar to postprandial plasma **amylin** concns. in normal volunteers. The plasma glucose, free insulin, glucagon, epinephrine and norepinephrine concns. during the insulin infusion test before and after therapy were identical in each of the groups. Prior to pramlintide therapy, Sustacal ingestion produced a 4.0-4.8 mmol/l rise in plasma glucose concns. in each of the groups. Pramlintide therapy reduced postprandial **hyperglycemia** as reflected by the 3-h incremental AUCglucose (AUCglucose above or below fasting glucose concn.) Day 1 vs Day 14: 30 .mu.g, 322 .+-. 92 vs -38 .+-. 161 mmol/l .sum. min, p = 0.010; 100 .mu.g, 317 .+-. 92 vs -39 .+-. 76 mmol/l .sum. min, p = 0.001; and 300 .mu.g, 268 .+-. 96 vs -245 .+-. 189 mmol/l .sum. min, p = 0.077. Thus, pramlintide therapy with these regimens did not appear to impair either in vivo insulin action or the counter-regulatory response to hypoglycemia but did show a clear effect of blunting postprandial **hyperglycemia** following a standardized meal.

L21 ANSWER 11 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
96:451813 Document No.: 99174169. **Amylin** response following sustacal ingestion is diminished in type II **diabetic** patients treated with insulin.. Fineman M S; Giotta M P; Thompson R G; **Kolterman O K**; Koda J E. Amylin Pharmaceutials Inc.,

San Diego, CA, USA Diabetologia32nd Annual Meeting of the European Association for the Study of Diabetes, Vienna, Austria, September 1-5, 1996., 39 (SUPPL. 1). 1996. A149. ISSN: 0012-186X. Language: English

AN 96:451813 BIOSIS

L21 ANSWER 12 OF 21 MEDLINE

97049741 Document Number: 97049741. Modulation of gastric emptying as a therapeutic approach to glycaemic control. Moyses C; Young A; **Kolterman O**. (Amylin Europe Ltd, Magdalen Centre, Oxford, UK.)DIABETIC MEDICINE, (1996 Sep) 13 (9 Suppl 5) S34-8. Ref: 19. Journal code: DME. ISSN: 0742-3071. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **Amylin** is a peptide hormone which is deficient in patients with Type 1 and late stage Type 2 **diabetes**. Evidence from studies in rats and humans has suggested that it is involved in glucose homeostasis by modulating gastric emptying and, possibly, by regulating the release of glucagon. These observations have led to the suggestion that **amylin** may be used clinically to improve glycaemic control in patients with **diabetes**. Preliminary studies with the human **amylin** analogue, pramlintide, have provided evidence of beneficial effects in terms of improved glycaemic control in these patients; these effects are currently being investigated in long term phase III studies.

L21 ANSWER 13 OF 21 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 6

1996:163350 Document No. 124:279659 Pharmacokinetics and pharmacodynamics of AC137 (25,28,29 tripro-**amylin**, human) after intravenous bolus and infusion doses in patients with insulin-dependent **diabetes**. Colburn, Wayne A.; Gottlieb, Alan B.; Koda, Joy; **Kolterman, Orville G.** (Harris Laboratories, Inc., Phoenix, AZ, 85040-2955, USA). J. Clin. Pharmacol., 36(1), 13-24 (English) 1996. CODEN: JCPCBR. ISSN: 0091-2700.

AB A study was conducted to evaluate the effect of 30-.mu.g, 100-.mu.g, and 300-.mu.g 2-min bolus doses and 2-h infusion doses of AC137 (25,28,29 tripro-**amylin**, human) on plasma AC137 concns. and plasma glucose and lactate responses in patients with insulin-dependent **diabetes** mellitus (IDDM). The study design was an imbedded two-way crossover wherein patients received placebo and active boluses in one period and placebo and active infusions in the other period. Two patients in each dose group received placebo throughout the two periods. Pharmacokinetics and pharmacodynamics (PK/PD) were detd. during the 6-h period after initiation of dosing. Data were fitted with a linked PK/PD model. Pharmacokinetics were linear over the dose range studied, and attenuation of glucose and lactate responses to a mixed meal was dose and concn. dependent. The results of the PK/PD model indicate that the attenuation of glucose and lactate responses was greater after AC137 infusion doses than after the same doses given as a bolus. Glucose and lactate responses to a mixed meal were essentially negated by the 300-.mu.g infusion dose.

L21 ANSWER 14 OF 21 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.

96290500 EMBASE Modulation of gastric emptying as a therapeutic approach to glycaemic control. Moyses C.; Young A.; **Kolterman O.**. Amylin Europe Limited, Magdalen Centre, Oxford Science Park, Oxford OX4 4GA, United Kingdom. Diabetic Medicine 13/SUPPL. 5 (S34-S38) 1996.
ISSN: 0742-3071. CODEN: DIMEEV. Pub. Country: United Kingdom.
Language: English. Summary Language: English.

AB **Amylin** is a peptide hormone which is deficient in patients with Type 1 and late stage Type 2 **diabetes**. Evidence from studies in rats and humans has suggested that it is involved in glucose homeostasis by modulating gastric emptying and, possibly, by regulating the release of glucagon. These observations have led to the suggestion that **amylin** may be used clinically to improve glycaemic control in patients with **diabetes**. Preliminary studies with the human **amylin** analogue, pramlintide, have provided evidence of beneficial effects in terms of improved glycaemic control in these patients; these effects are currently being investigated in long term phase III studies.

L21 ANSWER 15 OF 21 CAPLUS COPYRIGHT 1998 ACS
1996:494503 Document No. 125:133727 Methods for treating gastrointestinal motility. **Kolterman, Orville G.**; Young, Andrew A.; Rink, Timothy J. (Amylin Pharmaceuticals, Inc., USA). S. African ZA 9406881 A 951030, 54 pp. (English). CODEN: SFXXAB. APPLICATION: ZA 94-6881 940907. PRIORITY: US 93-118381 930907.
AB In 24 male subjects with insulin-dependent **diabetes** mellitus, the **amylin** agonist **AC 0137** (30, 100, or 300 .mu.g, i.v.) dose-dependently decreased postprandial **hyperglycemia**. **Amylin** agonists may be useful in inhibiting gastrointestinal motility, as during magnetic resonance imaging diagnostic procedures, postprandial dumping syndrome, or postprandial **hyperglycemia**. **Amylin** antagonists, such as acetyl-9-32-[Arg11,18,Asn30,Tyr32]-salmon calcitonin can be used to accelerate gastric emptying as during **diabetic** neuropathy or anorexia nervosa.

L21 ANSWER 16 OF 21 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-123240 [16] WPIDS
AB WO 9507098 A UPAB: 950502
An **amylin** or an **amylin** agonist or **amylin** agonist analogue is administered to beneficially regulate gastrointestinal motility, to treat post-prandial dumping syndrome or to treat post-prandial hyperglycaemia.

An **amylin** antagonist is administered to treat gastric hypomotility or to accelerate gastric emptying.

USE - The **amylin** or agonist or analogue may be used to reduce gastric motility or to delay gastric emptying e.g. in a subject undergoing a gastrointestinal diagnostic procedure such as a radiological examination or magnetic resonance imaging. The gastric motility may be associated with a gastrointestinal disorder such as spasm, e.g. spasm associated with a disorder selected from acute diverticulitis or a disorder of the biliary tract or a disorder of the Sphincter or Oddi. The post-prandial hyperglycaemia may be a consequence of type 2 **diabetes** mellitus.

The **amylin** may also be used to treat ingestion of a toxin by administering an amount effective to prevent or reduce the passage of stomach contents to the intestines then aspirating the stomach contents.

The hypomotility for which the antagonist is used may be a consequence of **diabetic** neuropathy or anorexia nervosa.

Effective daily anti-emptying doses of cpds. such as 18Arg25 28Pro-L-**amylin**, des-1Lys18Arg25 28Pro-L-**amylin**, 18Arg25 28 29Pro-L-**amylin**, des-1Lys18Arg-25 28 29Pro-L-**amylin**, 25 28 29Pro-L-**amylin**, des-1Lys25 28 29Pro-L-**amylin** and 25Pro26Val25 28Pro-L-**amylin** are typically in the range 0.01 or 0.03 to 5 mg/day, most pref. 0.01 or 0.1 to 1 mg/day for a 70 kg patient, administered in a single or

divided doses.

Administration may be by injection, pref. s.c. or i.m. Oral administration, increasing dosages 5-10 fold, may also be used.

Amylin antagonists may be administered in a dosage of 0.1-30 mg/day, most pref. 0.1-3 mg/day by injection, or orally with a 5-10 fold dosage increase.

Dwg.0/17

L21 ANSWER 17 OF 21 MEDLINE DUPLICATE 7

96002761 Document Number: 96002761. Reduction of postprandial **hyperglycemia** in subjects with IDDM by intravenous infusion of AC137, a human **amylin** analogue. **Kolterman O G** ; Gottlieb A; Moyses C; Colburn W. (Amylin Pharmaceuticals, San Diego, California 92121, USA..)DIABETES CARE, (1995 Aug) 18 (8) 1179-82. Journal code: EAG. ISSN: 0149-5992. Pub. country: United States. Language: English.

AB OBJECTIVE--To demonstrate that intravenous administration of AC137 (25,28,29 tripro-human **amylin**), a human **amylin** analogue, modulates the rate of appearance of glucose derived from a standard oral meal in the peripheral circulation of patients with insulin-dependent **diabetes** mellitus (IDDM). RESEARCH DESIGN AND METHODS--After the observation that a 2-h infusion of AC137 at a rate of 150 micrograms/h, in conjunction with the subjects' usual morning insulin dose, decreased postprandial **hyperglycemia** in 6 subjects with IDDM, a double-blind placebo-controlled two-period crossover design in an additional 18 IDDM patients was undertaken to confirm and extend the observation. Based on reasoning that an effect to modulate the appearance of orally administered glucose would have no impact on the disposition of an intravenous glucose load, nine patients were challenged with an intravenous glucose loads (300 mg/kg), while another nine patients were challenged with a standardized Sustacal meal (350 kcal) during a 5-h infusion of AC137 (50 micrograms/h). On each occasion, the subjects received their usual morning doses of insulin subcutaneously. The impact of the AC137 infusion on the plasma glucose responses to these different challenges was assessed. RESULTS--Intravenous infusion of AC137 yielding steady state plasma concentrations of 225 +/- 15 pmol/l (mean +/- SE) reduced postprandial plasma glucose concentrations after the standardized Sustacal meal challenge. The mean area under the glucose curve, corrected for baseline, was reduced from -1,869 +/- 5,562 mg.dl-1.min during placebo infusion to -28,872 +/- 4,812 mg.dl-1.min during AC137 infusion, P = 0.0015. In contrast, an AC137 infusion producing steady-state concentrations of 234 +/- 16 pmol/l had no effect on the plasma glucose profile after administration of an intravenous glucose load. CONCLUSIONS--AC137 administration, in these patients with IDDM, reduced postprandial **hyperglycemia** apparently by affecting the delivery rate of glucose from the gastrointestinal tract. AC137 may prove to be a clinically useful addition to insulin regimens to facilitate the achievement of glycemic control.

L21 ANSWER 18 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS

95:425356 Document No.: 98439656. Reduction of postprandial **hyperglycemia** in patients with type II **diabetes** by the human **amylin** analogue AC137.. **Kolterman O G**; Gottlieb A B; Organ K A; Thompson R G. Amylin Pharmaceuticals Inc., 9373 Towne Centre Drive, San Diego, CA 92121, USA Diabetologia31st Annual Meeting of the European Association for the Study of Diabetes, Stockholm, Sweden, September 12-16, 1995., 38 (SUPPL. 1). 1995. A193. ISSN: 0012-186X. Language: English

AN 95:425356 BIOSIS

L21 ANSWER 19 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
94:145508 Document No.: 97158508. Infusion of **amylin** agonist, **AC-0137**, Reduces postprandial **hyperglycemia** in subjects with type I **diabetes** (IDDM).. **Kolterman O**; Kisicki J C; Peltier L; Gottlieb A; Moyses C. Amylin Pharmaceuticals Inc., San Diego, CA, USA Clinical ResearchJoint Meeting of the Western Society for Clinical Investigation, Western Section of the American Federation for Clinical Research, Western Society for Pediatric Research, Western Region of the Society for Investigative Dermatology and the Western Student Medical Research Committee, Carmel, California, USA, February 9-12, 1994., 42 (1). 1994. 87A. ISSN: 0009-9279. Language: English
AN 94:145508 BIOSIS

L21 ANSWER 20 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
94:462547 Document No.: 97475547. Administration of tripro-**amylin** reduces postprandial **hyperglycemia** in subjects with juvenile-onset **diabetes**.. **Kolterman O G**; Gottlieb A B; Moyses C J. Amylin Pharmaceuticals Inc., 9373 Towne Centre Drive, San Diego, CA, USA Diabetologia30th Annual Meeting of the European Association for the Study of Diabetes, Duesseldorf, Germany, September 27-October 1, 1994., 37 (SUPPL. 1). 1994. A72. ISSN: 0012-186X. Language: English
AN 94:462547 BIOSIS

L21 ANSWER 21 OF 21 BIOSIS COPYRIGHT 1998 BIOSIS
94:462445 Document No.: 97475445. Human **amylin** increases plasma renin in man: A possible link between hypertension and insulin resistance?. McNally P G; Phillips P A; Johnston C I; **Kolterman O G**; Cooper M E. Dep. Med., Univ. Melbourne, Austin Hosp., VIC 3084, AUL Diabetologia30th Annual Meeting of the European Association for the Study of Diabetes, Duesseldorf, Germany, September 27-October 1, 1994., 37 (SUPPL. 1). 1994. A46. ISSN: 0012-186X. Language: English
AN 94:462445 BIOSIS

L22 47 FILE CAPLUS
L23 46 FILE BIOSIS
L24 59 FILE MEDLINE
L25 57 FILE EMBASE
'CN' IS NOT A VALID FIELD CODE
L26 15 FILE WPIDS
L27 23 FILE USPATFULL

TOTAL FOR ALL FILES
L28 247 (OBES? OR OVERWEIGHT) AND (L1 OR AMYLIN?)

=> s l28 and (treat? or preven?)

L29 20 FILE CAPLUS
L30 6 FILE BIOSIS
L31 14 FILE MEDLINE
L32 16 FILE EMBASE
L33 14 FILE WPIDS
L34 23 FILE USPATFULL

TOTAL FOR ALL FILES
L35 93 L28 AND (TREAT? OR PREVEN?)

=> s l35 not l20

L36 20 FILE CAPLUS
L37 6 FILE BIOSIS
L38 14 FILE MEDLINE
L39 16 FILE EMBASE
L40 14 FILE WPIDS
L41 23 FILE USPATFULL

TOTAL FOR ALL FILES
L42 93 L35 NOT L20

=> s l42 and (agonist analog? or pro(3w)amylin or agonist)

L43 2 FILE CAPLUS
L44 1 FILE BIOSIS
L45 1 FILE MEDLINE
L46 4 FILE EMBASE
L47 3 FILE WPIDS
L48 15 FILE USPATFULL

TOTAL FOR ALL FILES
L49 26 L42 AND (AGONIST ANALOG? OR PRO(3W) AMYLIN OR AGONIST)

=> dup rem l49

PROCESSING COMPLETED FOR L49
L50 22 DUP REM L49 (4 DUPLICATES REMOVED)

=> d cbib abs 1-22

L50 ANSWER 1 OF 22 USPATFULL
1998:14479 **Treatment** of type 2 diabetes mellitus.
Cooper, Garth J.S., Woodstock, England
Greene, Jr., Howard, Rancho Santa Fe, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5716619 980210
APPLICATION: US 94-295361 940823 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antibody methods for blocking the effects of diabetes-associated peptide, or "**amylin**", a hormone found in the amyloid masses of Type 2 diabetics, are disclosed. This putative hormone has been discovered to function both to inhibit insulin secretion and to inhibit glycogen synthesis. Regulation is accomplished by blocking the binding of **amylin** or **amylin agonists**, including calcitonin gene related peptide (CGRP), or biologically active sub-peptides thereof. Inhibitors include antibodies directed to **amylin** and **amylin agonist** active sites. Other antagonists include anti-idiotype antibodies directed to antibodies directed to **amylin**.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 2 OF 22 USPATFULL
1998:6946 Polynucleotides that encode the calcitonin gene-related peptide receptor coponent factor (HOUNDC44).

Adamou, John E., Exton, PA, United States
Elshourbagy, Nabil, West Chester, PA, United States
SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
US 5710024 980120
APPLICATION: US 96-686178 960723 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Human CGRP-RCF polypeptides and DNA (RNA) encoding such CGRP-RCF and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such CGRP-RCF for the **treatment** of diabetes, migrane, pain and inflammation, Parkinson's disease, acute heart failure, hypotension, urinary retention, osteoporosis, hypertension, angina pectoris, myocardial infarction, ulcers, asthma, allergies, psychosis, depression, vomiting, benign prostatic hypertrophy, Paget's disease, **obesity**, cancer, gigantism and the like. Antagonists against such CGRP-RCF and their use as a therapeutic to **treat** diabetes, migrane, pain and inflammation, Parkinson's disease, acute heart failure, hypotension, urinary retention, osteoporosis, hypertension, angina pectoris, myocardial infarction, ulcers, asthma, allergies, psychosis, depression, vomiting, benign prostatic hypertrophy, Paget's disease, **obesity**, cancer, gigantism and the like are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the CGRP-RCF and for detecting altered levels of the polypeptide in a host.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 3 OF 22 USPATFULL
97:94212 Methods and compositions for **treating** pain with **amylin** or **agonists** thereof.
Young, Andrew A., San Diego, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5677279 971014
APPLICATION: US 96-767169 961216 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for **treating** pain are disclosed which comprise administration of a therapeutically effective amount of an **amylin** or an **amylin agonist** alone or in conjunction with a narcotic analgesic or other pain relief agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 4 OF 22 USPATFULL
97:36292 Selective **amylin** antagonist peptides and uses therefor
.
Gaeta, Lori, Olivenhain, CA, United States
Beaumont, Kevin, San Diego, CA, United States
Prickett, Kathryn, San Diego, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5625032 970429
APPLICATION: US 93-96172 930721 (8)

DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Peptides that inhibit **amylin** activity and that exhibit selectivity for **amylin** receptors relative to calcitonin and CGRP receptors are provided. These peptides may be used in the **treatment** of conditions where it is of benefit to reduce **amylin** activity, including the **treatment** of Type 2 diabetes mellitus, impaired glucose tolerance, **obesity**, insulin resistance and hypertension.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 5 OF 22 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
97197511 EMBASE Insulin and lipid metabolism: New developments in drug therapy. Mackay A.J.; Petrie J.R.. J.R. Petrie, Dept. of Medicine/Therapeutics, Western Infirmary, Glasgow G11 6NT, United Kingdom. Expert Opinion on Investigational Drugs 6/6 (665-675) 1997.
Refs: 84.
ISSN: 1354-3784. CODEN: EOIDER. Pub. Country: United Kingdom.
Language: English. Summary Language: English.
AB Current **treatments** for non-insulin-dependent diabetes mellitus (NIDDM) remain far from ideal. The presence of both hyperinsulinaemia and resistance to insulin action in NIDDM challenges the rationale of **treatments** which primarily boost insulin secretion. Novel therapeutic strategies focus mainly on increasing peripheral sensitivity to endogenous insulin, an approach which has the potential not only to **treat**, but also to **prevent** NIDDM in high-risk individuals. The most promising new agents are the thiazolidinedione derivatives, in particular troglitazone. Thiazolidinediones are ligands for a specific subtype of the peroxisome proliferator activated receptor (PPAR), and decrease plasma glucose levels in both **obesity** and NIDDM, while at the same time reducing circulating insulin and free fatty acid levels. The current development status of these agents is reviewed, along with an assessment of their potential in the **prevention** and **treatment** of diverse pathophysiological states characterised by insulin resistance, including atherosclerosis and polycystic ovarian disease. Reference is made to the current status of other experimental agents including hydantoin derivatives, .beta.3-adrenoceptor **agonists**, and inhibitors of lipolysis.

L50 ANSWER 6 OF 22 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1
1997:431135 Document No. 127:104300 The pharmacologic approach to the **treatment** of **obesity**. Weiser, Mitchell; Frishman, William H.; Michaelson, M. Dror; Abdeen, M. Anwar (Department of Medicine, The Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, 10461, USA). J. Clin. Pharmacol., 37(6), 453-473 (English) 1997. CODEN: JCPCBR. ISSN: 0091-2700. Publisher: Lippincott-Raven.
AB **Obesity** is a major risk factor for morbidity and mortality, and a series of pharmacol. approaches are available for helping to manage the problem. **Obesity** is caused by an imbalance between caloric intake and energy expenditure, which is influenced by both environmental and genetic factors. Pharmacol. **treatments** include anorexigenic agents, which fall into two broad categories: those that act via brain cotecholamine pathways and those that act via serotonin pathways. The most recent oral agents approved are dexfenfluramine, which is currently being marketed, and sibutramine. Both agents inhibit the control reuptake

of serotonin but in addn. may have effects on thermogenesis. Under investigation are agents that increase energy expenditure: the .beta.3-adrenergic receptor **agonists** and drugs that **prevent** the intestinal absorption of free fatty acids and cholesterol. In development are innovative approaches to influence leptin and its receptors, various **obesity** genes, and biol. substances thought to influence satiety (neuropeptide Y, enterostain, cholecystokinin, bombesin, and **amylin**). **Obesity** has now become a major target for drug development not only for affecting **obesity** per se but also for managing and **preventing** comorbid conditions such as diabetes and cardiovascular disease.

L50 ANSWER 7 OF 22 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2
1997:437791 Document No. 127:104380 Potential role of neuropeptide ligands in the **treatment** of overeating. Rowland, Neil E.; Kalra, Satya P. (Department of Psychology, University of Florida, Gainesville, FL, USA). CNS Drugs, 7(6), 419-426 (English) 1997. CODEN: CNDREF. ISSN: 1172-7047. Publisher: Adis.

AB A review, with 77 refs., on the role of various neuropeptides in controlling eating behavior and the prospects for ligands of these signaling systems in the **treatment** of eating disorders, in particular overeating and **obesity**. Neuropeptide Y is the most well known appetite-stimulating peptide. It is believed to exert this action through either Y1 or Y5 receptor subtypes in the hypothalamus. Selected antagonists with high affinity for these subtypes reduce food intake in animals, and so suggest that the development of clin. useful analogs may be possible. Galanin, another appetite-stimulating peptide, has been less well studied and the development of antagonists for galanin receptors is less well advanced. Studies using combinations of neuropeptide Y and galanin receptor antagonists, that may target carbohydrate and fat intake, resp., have not yet been reported. Several peptides are known to inhibit food intake. **Agonists** of receptors for these peptides that have a long duration of action could be useful appetite suppressants. These peptides include gut peptides such as cholecystokinin and glucagon-like peptide, and pancreatic peptides such as **amylin** and insulin. Recently, the **obesity** (ob/ob) gene-related peptide leptin has been proposed as an endogenous signaling system that regulates fat intake, and a novel analog of leptin has been shown to reduce food intake in rats. These peptides are thought to act on feeding-related regions at various levels of the neuraxis, prominently including the nucleus of the solitary tract, the lateral parabrachial nucleus, the paraventricular hypothalamus and the amygdala.

L50 ANSWER 8 OF 22 USPATFULL
96:111541 **Amylin** antagonist peptides and uses therefor.
Albrecht, Elisabeth, San Diego, CA, United States
Jones, Howard, Poway, CA, United States
Gaeta, Laura S. L., La Jolla, CA, United States
Prickett, Kathryn S., San Diego, CA, United States
Beaumont, Kevin, San Diego, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5580953 961203
APPLICATION: US 91-794288 911119 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds which inhibit **amylin** activity are provided. These compounds may be used in the **treatment** of

conditions where it is of benefit to reduce **amylin** activity, including the **treatment** of Type 2 diabetes mellitus, impaired glucose tolerance, **obesity** and insulin resistance.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 9 OF 22 USPATFULL
95:52437 Synthetic preparation of **amylin** and **amylin** analogues.
Lehman de Gaeta, Laura S., 8126 Camino del Sol, La Jolla, CA, United States 92037
Albrecht, Elisabeth, 10540 Bannister Way, San Diego, CA, United States 92126
US 5424394 950613
APPLICATION: US 93-90361 930708 (8)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Synthetic **amylin** and **amylin** analogs which have high biological activity and which are substantially free from deletion peptides and other contaminating peptides are provided. Also provided are methods for the solid phase peptide synthesis of **amylin** and **amylin** analogs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 10 OF 22 USPATFULL
95:31855 **Treatment** of bone disorders.
MacIntyre, Iain, Heathfield, England
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5405831 950411
APPLICATION: US 93-98015 930727 (8)
PRIORITY: GB 89-15712 890708
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Use of **amylin**, or variants of **amylin**, as well as **amylin agonists**, for the **treatment** of bone disorders, in particular osteoporosis, Paget's disease, and malignant deposits in bone, bone loss of malignancy or endocrine disorders or autoimmune arthritides or immobility and disuse, and in other conditions where a hypocalcaemic effect is of benefit. Functional peptide fragments of **amylin**, or a variant of **amylin** or **amylin** fragment, are provided as well as a soluble **amylin**, **amylin** fragments, or variants thereof, or a lyophilized product, or an oral formulation for use alone, or in combination with other agents, including insulin (or insulin-stimulating agents, including but not limited to the sulfonylureas) and estrogens, for the **treatment** of disorders of bone or calcium balance.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 11 OF 22 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 94-316927 [39] WPIDS
AB WO 9421665 A UPAB: 941122
(A) An assay method for use in identifying, screening for, evaluation or characterising C1a or C1b receptor binding cpds. (RBCs) comprises (a) bringing together a test sample and a C1a or C1b receptor prepn. contg. a C1a or C1b receptor protein (RP), the test sample contg. one or more test cpds., (b) incubating the test

sample and the receptor prepn. to permit the binding of a C1a or C1b RBC to the C1a or C1b RP and (c) identifying those test samples contg. one or more test cpds. which detectably bind to the C1a or C1b receptor.

Also claimed are: (B) an assay for evaluating one or more receptor binding characteristics sought to be detd. for a known or candidate calcitonin or **amylin** or calcitonin gene related peptide (CGRP) **agonist** or antagonist cpd., which comprises (a) bringing together a test sample and a C1a or C1b receptor prepn. contg. a C1a or C1b RP, the test sample contg. one or more test cpds., (b) incubating the test sample and the receptor prepn. to permit binding of a C1a or C1b receptor binding ligand to the C1a or C1b RP and (c) assessing or measuring the ability of the cpd. to compete against a labelled ligand for binding to the C1a or C1b receptor prepn.; (C) purified C1a receptor; (D) purified C1b receptor; (E) purified nucleic acid encoding a C1a receptor or C1b receptor; (F) a vector contg. nucleic acid encoding a C1a receptor or C1b receptor; (G) cells transfected with nucleic acid or a vector contg. nucleic acid encoding a C1a receptor or C1b receptor.

USE - The C1a or C1b RPs can be used for determining the presence or amt. of or sepg. C1a or C1b RBCs in a sample (claimed). They can also be used for producing antibodies (claimed). The C1a or C1b RBCs can be used for screening a biological substance for the presence of C1a or C1b receptors (claimed). The C1a and C1b RPs are used esp. for identifying calcitonins, **amylin** or CGRP **agonists** or antagonists for **treating** conditions such as **obesity**, anorexia, pain, diabetes mellitus impaired glucose tolerance or insulin resistance.

Dwg.0/8

L50 ANSWER 12 OF 22 USPATFULL

94:113002 Methods for **treating** renin-related disorders with **amylin** antagonists.

Young, Andrew A., San Diego, CA, United States
Rink, Timothy J., La Jolla, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5376638 941227
APPLICATION: US 92-939106 920901 (7)
DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for **treating** conditions associated with elevated, inappropriate or undesired renin activity are disclosed which comprise administration of an effective amount of any **amylin** antagonist alone or in conjunction with other anti-hypertensive agents. Methods for screening for and/or evaluating anti-renin **amylin** antagonists are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 13 OF 22 USPATFULL

94:99894 **Treatment** of **obesity** and essential hypertension and related disorders.

Cooper, Garth J. S., Solana Beach, CA, United States
Leighton, Brendan, Eynsham, England
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5364841 941115
APPLICATION: US 93-81033 930621 (8)
DOCUMENT TYPE: Utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The administration of antagonists and blockers of **amylin** or CGRP or both for the **treatment** of **obesity** and essential hypertension and associated lipid disorders and atherosclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 14 OF 22 USPATFULL
94:7674 **Treatment** of insulin resistance.
Cooper, Garth J. S., Woodstock, England
Greene, Jr., Howard, Rancho Sante Fe, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5281581 940125
APPLICATION: US 92-901602 920619 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds and methods for blocking the effects of diabetes-associated peptide, or "**amylin**", a hormone found in the amyloid masses of Type 2 diabetics. This putative hormone has been discovered to function both to inhibit insulin secretion and to inhibit glycogen synthesis. Regulation is accomplished by blocking the binding of **amylin** or **amylin agonists**, including calcitonin gene related peptide (CGRP], or biologically active sub-peptides thereof. Inhibitors include substituted peptides or sub-peptides of **amylin** or CGRP, cross-linked **amylin** and **amylin agonists**, synthetic **amylin**, anti-**amylin** receptor antibodies and anti-idiotype antibodies, and antibodies directed to **amylin** and **amylin agonist** active sites. Other antagonists include organic compounds which can be screened and assayed for anti-**amylin** effects by disclosed methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 15 OF 22 USPATFULL
94:5868 **Treatment** of **obesity** and essential hypertension and related disorders.
Cooper, Garth J. S., Solana Beach, CA, United States
Leighton, Brendan, Eynsham, England
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5280014 940118
APPLICATION: US 91-737794 910718 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The administration of antagonists and blockers of **amylin** or CGRP or both for the **treatment** of **obesity** and essential hypertension and associated lipid disorders and atherosclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 16 OF 22 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
94337484 EMBASE Methods for **treating** renin-related disorders with **amylin** antagonists. EXPERT OPIN. THER. PAT. 4/11 (1383-1384) 1994.
ISSN: 1354-3776. CODEN: EOTPEG. Pub. Country: United Kingdom.
Language: English. Summary Language: English.

RM 300.E9

AB Previously described **amylin** antagonists are claimed to ameliorate renin activity in subjects and have potential for the **treatment** of diseases such as congestive heart failure, syndrome X and hypertension. The **amylin** antagonists are peptidic in nature and selective for the **amylin** receptor over the calcitonin and/or calcitonin gene related peptide (CGRP) receptors. In WO 9405317 [101], subcutaneous administration of 100 .mu.g of synthetic rat **amylin** to rats led to a 3 to 4-fold increase in plasma renin activity versus control levels that was statistically significant over the 4 hour duration of the experiment. Plasma renin activity was determined by specific radioimmunoassay for the generation of angiotensin I expressed as ng/ml/hr. Administration of an **amylin** receptor specific antagonist, such as Ac-[Asn30, Tyr32]-calcitonin(8-32)(salmon), at t = -30 min (iv bolus) followed by a 1.0 mg/hr continuous iv infusion until t = 120 min blocked the increase in plasma renin activity induced by the above dose of rat **amylin**. Similar results were obtained for other **amylin** antagonists, such as calcitonin(8-32)(salmon) and Ac-[Glu15, Arg18, Val27, Asn30, Tyr32]-**amylin**(8-18)(human) calcitonin(19-32)(salmon). The chemistry for the preparation of the **amylin** antagonists is not exemplified, however it can be assumed that standard solid phase peptide synthetic methodology is utilised as described in previous patent applications by this group [102-104]. Their structures are as follows: Ac4[Asn30, Tyr32]-calcitonin(8-32)(salmon): Ac-Val8-Leu-Gly10-Lys-Leu-Ser-Gln-Glu15-Leu-His-Lys-Leu-Gln20-T hr-Tyr-Pro-Arg-Thr25-Asn-Thr-Gly-Ser-Asn30-Thr-Tyr32-NH2. Ac-[Glu15, Arg18, Val27, Asn30, Tyr32]-**amylin**(8-18)(human) calcitonin(19-32)(salmon): Ac-Ala8-Thr-Gln10-Arg-Leu-Ala-Asn-Glu15-Leu-Val-Arg-Leu-Gln20-T hr-Tyr-Pro-Arg-Thr25-Asn-Val-Gly-Ser-Asn30-Thr-Tyr32-NH2. In the US patent application [105], calcitonins of avian or teleost origin, particularly from chicken, eel or salmon are referred to. In assays, ultimobranchial calcitonins were found to have very high affinity for **amylin** receptors and to be potent inhibitors of insulin-stimulated glycogen synthesis and stimulators of glycogen breakdown in isolated rat soleus muscle. In an example from tabulated results, chicken calcitonin gave an IC50 value of 0.03 nM for receptor binding and an EC50 value of 0.7 nM for soleus muscle. In in vitro assays on rats, it was found that **amylin** and calcitonin both increase plasma glucose in a similar and dose-dependent manner, and synergy was noted between glucagon and salmon calcitonin. The final patent [106] deals with a novel diagnostic for **amylin agonists** and **amylin** antagonists for the **treatment** of diabetes mellitus, **obesity** and hypertension.

L50 ANSWER 17 OF 22 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 93-386486 [48] WPIDS
AB WO 9323435 A UPAB: 940120
(A) A monoclonal antibody (MAb) is claimed which binds to the C-terminal end of human **amylin**.

Also claimed are (B) a MAb which binds to the amidated C-terminal end of human **amylin** and not to the non-amidated C-terminal end; (C) an assay using a MAb for detecting the presence or amt. of an **amylin** analogue, comprising (a) contacting the **amylin** analogue or a sample suspected of contg. the analogue with the MAb and (b) determining the presence or amt. of the **amylin** analogue, where the MAb binds to the C-terminal end of human **amylin**; (D) a kit comprising a MAb as in (A) or (B).

USE/ADVANTAGE - The MAbs can be used for the specific detection

of human **amylin** or analogues. In partic., they can differentiate between C-terminal amidated human **amylin** and the inactive non-amidated human **amylin**. They can be used for monitoring **amylin** levels in Type 1 diabetics, in Type 2 diabetics and **obese** individuals and in other conditions in which **amylin** levels may be altered. The MAbs can also be used for measuring levels of **amylin** analogues, such as 25, 28, 29 **Pro**-human **amylin** (AC-0137), which are being evaluated for use in the **treatment** of Type 1 diabetes.
Dwg.0/0

L50 ANSWER 18 OF 22 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 93-243368 [30] WPIDS
AB WO 9314408 A UPAB: 931118
A new assay method for use in identifying or screening for myotonin receptor (MR) binding cpds. (MRBCs) comprising (a) bringing together a test sample and a MR prepn., the test sample contg. one or more test cpds. and the MR prepn. contg. a MR protein which binds calcitonin or an **amylin agonist** or antagonist, (b) incubating the test sample and the MR prepn. under conditions which permit the binding of calcitonins or an **amylin agonist** or antagonist to the MR protein, and (c) identifying those test samples contg. one or more test cpds. which detectably bind to the MR.

The assay may use ligands such as **amylin**, calcitonin, alpha-calcitonin gene related peptide (CGRP) or beta-CGRP. Ligands may be labelled using e.g. 125I or biotin.

USE - The MR is useful for identifying, screening and characterising cpds. useful for the **treatment** of hypoglycemic conditions or diseases characterised by insulin resistance such as Type 2 diabetes mellitus, **obesity** and hypertension. The MR and MR-specific antibodies can also be used for diagnosis.
Dwg.1/7

L50 ANSWER 19 OF 22 USPATFULL
93:100737 **Treatment** of type 2 diabetes mellitus.
Cooper, Garth J. S., Woodstock, United Kingdom
Greene, Jr., Howard, Rancho Santa Fe, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5266561 931130
APPLICATION: US 91-715302 910604 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds and methods for blocking the effects of diabetes-associated peptide, or "**amylin**", a hormone found in the amyloid masses of Type 2 diabetics. This putative hormone has been discovered to function both to inhibit insulin secretion and to inhibit glycogen synthesis. Regulation is accomplished by blocking the binding of **amylin** or **amylin agonists**, including calcitonin gene related peptide (CGRP], or biologically active sub-peptides thereof. Inhibitors include substituted peptides or sub-peptides of **amylin** or CGRP, cross-linked **amylin** and **amylin agonists**, synthetic **amylin**, anti-**amylin** receptor antibodies and anti-idiotype antibodies, and antibodies directed to **amylin** and **amylin agonist** active sites. Other antagonists include organic compounds which can be screened and assayed for

anti-**amylin** effects by disclosed methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 20 OF 22 USPATFULL
93:98316 Receptor-based screening methods for **amylin** **agonists** and antagonists.
Beaumont, Kevin, San Diego, CA, United States
Rink, Timothy J., San Diego, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5264372 931123
APPLICATION: US 91-670231 910315 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for identifying or screening or characterizing or assaying or isolating known or candidate **agonists** and antagonists of **amylin**, comprising binding assays utilizing preparations containing specific receptors for **amylin**. Membranes from the brain that contain high density receptors for **amylin** are particularly useful for the methods of this invention, and as a source of **amylin** receptors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 21 OF 22 USPATFULL
93:93765 Hypoglycemics.
Cooper, Garth J. S., Solana Beach, CA, United States
Moore, Candace X., San Diego, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5260275 931109
APPLICATION: US 90-567919 900814 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Non-insulin dependent, or type 2, diabetes mellitus in a patient is **treated** by administering to the patient a hypoglycemic agent that enhances plasma concentrations of **amylin** and a therapeutically effective amount of an **amylin** antagonist. Hypoglycemic agents which enhance plasma concentrations of **amylin** can be sulfonylureas such as glibenclamide and tolbutamide. **Amylin** antagonists can be **amylin** 8-37 and CGRP 8-37. Administration of the **amylin** antagonist in conjunction with the hypoglycemic agent also enhances the blood glucose lowering effects of the hypoglycemic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L50 ANSWER 22 OF 22 USPATFULL
93:65378 Hyperglycemic compositions.
Young, Andrew, San Diego, CA, United States
Cooper, Garth J. S., Solana Beach, CA, United States
Amylin Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)
US 5234906 930810
APPLICATION: US 91-640478 910110 (7)
DOCUMENT TYPE: Utility.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions having **amylin** or an **amylin** **agonist** and a glucagon compound, particularly peptide

compounds, for the control of glucose production in mammals are provided. The compositions are useful in the **treatment** of hypoglycemia, including acute hypoglycemic conditions such as those brought on by insulin overdose and the overuse of oral hypoglycemic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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